Prospective observational study of post-operative infection and outcomes after non-cardiac surgery: Analysis of prospective data from the VISION cohort

Running title: Risk factors and outcomes of post-operative infection

Y. I. Wan,[1] A. Patel,[1] T. E. F. Abbott,[1] C. Achary,[2] N. MacDonald,[2] E. Duceppe,[3] D. I. Sessler,[4] W. Szczeklik,[5] G. L. Ackland,[1] P. J. Devereaux,[6] and R. M. Pearse.[1]

1. William Harvey Research Institute, Queen Mary University of London, UK EC1M 6BQ.
2. Barts Health NHS Trust, London E1 1BB.
3. Department of Medicine, Centre Hospitalier de l'Universite de Montreal, Montreal, Canada
4. Department of Outcomes Research, Anesthesiology Institute, Cleveland Clinic, Ohio
5. Dept of Intensive Care and Perioperative Medicine, Jagiellonian Universtiy Medical College, Krakow, Poland
6. McMaster University and Population Health Research Institute, Hamilton, Ontario, Canada

Correspondence to:
Professor Rupert M. Pearse
Adult Critical Care Unit
Royal London Hospital
London
E1 1BB
United Kingdom
email: r.pearse@qmul.ac.uk
Tel: +44 20 3594 0351

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Summary

Background

Infection is a frequent cause of post-operative morbidity and mortality. The incidence, risk factors, and outcomes for post-operative infections remain poorly characterised.

Methods

This is a secondary analyses of a prospective international cohort study of patients aged ≥45 years who had non-cardiac surgery (VISION) including data describing infection within 30 days after surgery. The primary outcome was post-operative infection. The secondary outcome was 30-day mortality. We used univariable and multivariable logistic regression to identify baseline risk factors for infection. Results are presented as n (%) or odds ratio (OR) with 95% confidence intervals (CI). Some denominators vary according to rates of missing data.

Results

Among 39,996 surgical patients, 3,905 (9.8%) experienced 5,152 post-operative infections and 715 (1.8%) died. The most frequent infection was surgical site infection (1,555/3,905 [39.8%]). Infection was most strongly associated with general surgery (OR 3.74 [3.11-4.49]; p<0.01) and open surgical technique (OR 2.03 [1.82-2.27]; p<0.01). 30-day mortality was greater amongst patients who experienced infection (262/3,905 [6.7%] vs 453/36,091 patients who did not [1.3%]; OR 3.47 [2.84-4.22]; p<0.01). Mortality was highest amongst patients with central nervous system infections (OR 14.72 [4.41-49.12]; p<0.01).

Conclusions

Infection is a common and important complication of non-cardiac surgery, which is associated with high mortality. Further research is needed to identify more effective measures to prevent infections after surgery.

Introduction

There are more than 310 million surgical procedures worldwide each year.[1] In the UK, one in ten adults has a surgical procedure each year, and the annual number of procedures is increasing steadily.[2] Estimates of post-operative morbidity and mortality vary, but approximately seven million patients worldwide experience a post-operative complication each year.[3-5] Post-operative infections increase morbidity and mortality, and prolong intensive care and hospital stays.[6, 7]

Post-operative infections are a common cause of post-operative death, although estimates of incidence vary widely. For example, organ space infection has reported mortality rates between 4 and 9%, and mortality ranges from 28 to 46% in those patients who develop septic shock.[8, 9] However, many post-operative infections do not cause severe sepsis or septic shock and the mode of death for such patients is unclear in many cases. The literature remains unclear about the overall rates of post-operative infection and subsequent outcomes.[10] Despite many studies focused on specific types of surgery, the relationships between different types of infection, surgical procedures, and other adverse outcomes are still not clearly defined.[11-13] Source control and antimicrobial therapy are the mainstays of treatment for post-operative infection. However widespread use of broad-spectrum agents has led to increasing concerns about antimicrobial resistance, which in itself carries a significant socioeconomic burden and a high mortality.[14, 15]

There are few large epidemiological studies that explore potential risk factors for and outcomes of post-operative infection. We therefore report a prospective analysis of data collected during the multi-national, prospective cohort study called the Vascular Events in Non-cardiac Surgery Patients Cohort Evaluation (VISION) study to evaluate risk factors for post-operative infection, the incidence of different types of infection, and subsequent morbidity and mortality.

Methods

Study cohort

This is a prospective analysis of data collected during the VISION study. The methods of this prospective international observational cohort study have been described in detail elsewhere.[16] The study was approved by institutional review boards or ethics committees at each site and was registered with ClincalTrials.gov (NCT00512109). Participants were aged 45 years or older and underwent non-cardiac surgery using general and/or regional anaesthesia, with at least an expected overnight hospital stay. Participants were approached for written informed consent before surgery. When this was not possible (e.g. before emergency surgery), written consent was sought within 24 hours after surgery. In eight sites, where patients had no next of kin and were unable to provide consent before surgery (e.g., trauma surgery cases), a deferred consent process was used.

Data collection

The dataset for these analyses includes all patients with outcome data restricted to 30 days after surgery. Detailed and standardised data were collected before surgery, during hospital stay until discharge and then at 30 days after surgery. Where an infection occurred, additional data were collected. Full definitions of the variables included in this analysis are documented in supplementary information.

Outcome measures

The primary outcome measure was infection within 30 days after surgery. Diagnosis of infection was made by clinical evidence meeting CDC/NHSN Surveillance definitions for specific types of infections.[17] Infection outcomes were graded by severity using Clavien-Dindo classification (supplementary file).[18, 19] The secondary outcome measure was 30-day mortality. As an exploratory objective, we also evaluated the association between post-operative infection and Myocardial Injury After Noncardiac Surgery (MINS) (supplementary file). To determine whether the presence of post-operative infection influenced the delivery of care, we used the following tertiary process measures: hospital length of stay and admission to intensive care.

Statistical analysis

A prospective statistical analysis plan was completed before commencing any analyses. All analyses were performed using Stata 15.1 (StataCorp, USA). Cases that were missing outcome data were excluded by list-wise deletion. We present descriptive statistics for baseline characteristics for patients with and without post-operative infection as well as different types of infection. For patients who had more than one incidence of infection, we included only the event with the highest Clavien-Dindo severity grading to prevent duplication of patients included in analyses. A number of patients had more than one category selected for type of surgery. We excluded these in the main analyses in order to evaluate impact of each type on infection risk. We then evaluated the impact of having more than one type of surgery separately. Categorical data are reported n (%). Normally distributed data are expressed as mean and standard deviation (SD), non-normally distributed data are expressed as median and interquartile range (IQR).

We used univariable and multivariable logistic regression analysis to test for association between post-operative infection within 30 days after surgery and known risk factors for perioperative morbidity and mortality. Post-operative infection was the dependent variable and the following risk factors were included as independent variables: age (<65, 65-85, ≥85 years), male sex, smoking status (never, ex-smoker, current smoker), body mass index (BMI) (<18.5, 18.5-24.9, ≥25, ≥30), co-morbidities (current atrial fibrillation, previous atrial fibrillation, congestive heart failure, coronary artery disease, cerebral vascular event, peripheral vascular disease, hypertension, chronic obstructive pulmonary disease, diabetes, active cancer), pre-operative haemoglobin level, pre-operative estimated glomerular filtration rate (eGFR) (<30, 30-44, 45-60, >60 ml min^{-1}), urgency of surgery (<72 hours, all other), type of surgery (vascular, general, thoracic, major urology or gynaecology, major orthopaedic, major neurosurgery, low risk surgery), surgical technique (endoscopic only, open), type of anaesthetic (general, regional, combined). Results of logistic regression analyses are presented as odds ratios (OR) with 95% confidence intervals (CI).

Secondary and tertiary analyses

To determine whether post-operative infection was associated with the secondary outcome measure defined as 30-day mortality, we conducted univariable and multivariable logistic regression analysis. We used post-operative infection within 30 days after surgery as the independent variable and 30-day mortality as the dependent variable. Models were corrected for previously identified covariates in the primary analysis. The outcome variables were categorised by presence of infection, type of infection, and severity of infection. Forest plots for risk of 30-day mortality show the impact of each infection type using univariable analyses.

We performed time-to-event analysis and provide Kaplan-Meier plots for the relationship between post-operative infection and mortality. To determine whether the presence of post-operative infection influenced delivery of care we used hospital length of stay as a tertiary process measure. We constructed univariable linear and logistic regression models with post-operative infection within 30 days after surgery as the independent variable and either hospital length of stay as the dependent variable. The results were presented as beta coefficients with 95% CI for the linear regression model.

Results

A total of 40,037 patients were recruited to the VISION study between August 6th 2007 and January 11th 2011, of whom 40,004 had baseline data available for inclusion into this study. We excluded 8 patients with missing outcome data for post-operative infection leaving 39,996 for inclusion in the primary analyses (supplementary figure 1: STROBE flow diagram). Post-operative infection within 30 days following surgery occurred in 3,905 (9.8%) patients. Baseline characteristics for all patients and patients categorised by presence of post-operative infection are presented in Table 1. The majority of patients in our cohort underwent low risk surgery (38.3%), general surgery (19.9%), and orthopaedic surgery (17.5%). The age of patients who developed post-operative infection was higher than those who did not. A higher proportion of patients with infection were current smokers or ex-smokers, had a co-morbidity, lower pre-operative haemoglobin, and lower pre-operative eGFR. Patients who developed infection were more likely to have undergone urgent surgery and open surgical technique.

Baseline characteristics for patients categorised by type of infection are presented in Table 2. A number of patients developed more than one infection. There was a total of 5,152 infection events among 3,905 patients. Surgical site infection (n=1555), urinary tract infection (n=1086), and pneumonia (n=771) were the most common types of infection. More than one in five patients who had an infection (n=843, 21.6%) experienced more than one infection during their hospital stay; 590 patients had two, 164 patients had three, 49 patients had four, 30 patients had five, and ten patients had more than five infections. Incidences listed as 'other' included infection types that did not fall under the other categories such as gastroenteritis, methicillin-resistant staphylococcus aureus (MRSA), and iatrogenic line infections. A greater proportion of patients who developed upper respiratory tract infection had a current or ex-smoker history (73.0%) compared to other types of infection ranging from 13.3% (central nervous system) to 62.1% (peritonitis).

In patients who developed infection, 35.8% had undergone a general surgical procedure. General surgery was the surgical category with the highest rate of infection (1400/7950 [17.6%]). Patients who did not develop post-operative infection most commonly underwent low risk surgery (35.9%). A number of patients had surgery that came under more than one category, 1,099 patients had two (2.7%), 66 patients had three (0.2%). These patients were excluded from our main analyses in order to test the effect different types of surgery had on development of infection. We then replaced the type of surgery variable with numbers of surgery performed and showed that having more than one category of surgery carried higher risk of post-operative infection compared to having only one category (supplementary table 1). Distribution of different types of infection varied between different types of surgery. The majority of patients who developed infection after general surgery had incision site (41.1%) and urinary tract (22.0%) infections.

The results of multivariable logistic regression analyses for predetermined baseline characteristics against development of post-operative infection are listed in Table 3. Development of post-operative infection was associated with increasing age (≥85 years OR 1.80 [1.51-2.15]; p<0.01), 65-85 years OR 1.23 [1.13-1.33]; p<0.01, both compared to <65 years), male sex (OR 1.12 [1.04-1.22]; p<0.01), smoking history (current smoker: OR 1.37 [1.22-1.54]; p<0.01; ex-smoker: OR 1.29 [1.18-1.40]; p<0.01). In this cohort, patients with a higher pre-operative haemoglobin levels had lower rates of post-operative infection (OR 0.90 [0.88-0.91] per gram unit rise; p<0.01). Patients at the extremes of BMI range had higher rates of post-operative infection compared to those within normal range (BMI 18.5-24.9): underweight (BMI <18.5) (OR 1.33 [1.11-1.60], p<0.01) and obese (≥30) (OR 1.11 [1.01-1.23]; p=0.03). Rates of infection was higher in patients with lower pre-operative eGFR <30 ml min^{-1} (OR 1.38 [1.17-1.63]; p<0.01) or 30-44 ml min^{-1} (OR 1.23 [1.05-1.44]; p=0.01) compared to >60 ml min^{-1}.

Rates of post-operative infection were higher in patients who had urgent surgery within 72 hours of acute event defined as an acute illness admission (OR 1.41 [1.26-1.58]; p<0.01), and an open surgical technique (OR 2.03 [1.82-2.27]; p<0.01). Compared to using general anaesthesia, regional anaesthesia was associated with lower post-operative infection rates both used alone (OR 0.78 [0.69-0.87]; p<0.01), or in a combined regional and general anaesthesia approach (OR 0.78 [0.65-0.95]; p=0.01).

Secondary analyses

Patients who developed post-operative infection had a higher 30-day mortality rate (OR 3.47 [2.82-4.22]; p<0.01). When categorised by infection type, statistically significant associations were observed for all types apart from surgical abscess, urinary tract infection, upper respiratory tract infection, and osteomyelitis. The highest mortality risks were with CNS infections (OR 14.72 [4.41-49.12]; p<0.01), and positive blood culture without a clear primary source (OR 9.06 [5.08-16.17]; p<0.01). Severe infection within Clavien-Dindo grading III and above was associated with higher mortality (OR 13.55 [10.80-17.01]; p<0.01). In the adjusted analyses, less severe infection within Clavien-Dindo grading I to II had lower mortality rates compared to no infection (OR 0.51 [0.33-0.79]; p<0.01) (Table 4). Presence of post-operative infection was associated with longer hospital length of stay (12.75 days [12.39-13.12]; p<0.01).

Discussion

The principal finding of this analysis is that one in ten patients developed an infection within 30 days of surgery, and one in five of these patients developed multiple infections. 30-day mortality rates were more than three times greater for surgical patients who experienced an infection. Surgical site infection, urinary tract infection and pneumonia were the most frequent events. Infection was most common among patients recovering from general surgery and those who had general anaesthesia. This could be related to the risk profile of surgery or could be causative from increased infective risks following general anaesthesia including procedures such as urinary catheterisation. The frequency with which different types of infection occur varied between different surgical specialities. Having multiple surgical categories also increased risk of post-operative infection. Multi-specialty involvement may imply a higher degree of surgical complexity, and therefore a higher risk of post-operative complications.

The strongest risk factors for infection were older age, smoking history, and co-morbid disease. This is important because the number of elderly patients undergoing surgery continues to rise, with one in five people in England aged ≥75 years undergoing surgery in 2015.[20] Patients who were either underweight or obese experienced more infections, as did patients with anaemia and impaired renal function. There have been a number of previously published studies measuring post-operative infection rates and outcomes. Most of them are within single surgical specialities or even specific procedures and focusing on reporting one type of infection only. Mostly commonly, these have been surgical site infection, urinary tract infections, and pneumonia because these infections are most frequent, with orthopaedic surgery being most often evaluated.[21, 22] The most extensively reported has been surgical site infection with rates ranging from 3% (multiple surgical categories combined, costs-analysis study) to 36% (otolaryngology, cohort study).[23, 24]

Our findings are consistent with identifying previously reported risk factors. Various pathophysiological consequences of smoking have been proposed to explain the increased development of infection, particularly surgical site infection. These include impaired early host cellular defences reducing the ability to control bacterial wound contamination and prolonged tissue acidosis.[25] For orthopaedic surgery joint replacement, evidence to support pre-operative modification of risk factors is strongest for diabetes and smoking.[26] Malnutrition has been thought to impair wound healing and prolong inflammation via mechanisms such as impaired fibroblast proliferation and collagen synthesis.[27] Patients undergoing primary hip and knee arthroplasty have previously had improved perioperative outcomes following neuraxial versus general anaesthesia including reduced infections.[28] Similarly, general anaesthesia for caesarean sections were also associated with a higher incidence of surgical site infection compared with neuraxial anaesthesia.[29] Furthermore, our findings support that from a meta-analysis of joint arthroplasty procedures showing lower rates of surgical site infection following neuraxial anaesthesia.[30] Conversely, the effects of co-morbidities such as coronary artery disease, hypertension, and diabetes have not been replicated following our adjusted analyses.[31, 32] This may reflect the fact the underlying mechanisms behind these co-morbidities may interact and therefore not demonstrate an effect due to loss of statistical power. The finding of less severe infection within Clavien-Dindo grading I to II on adjusted analyses having lower mortality rates compared to no infection is a likely artefact due to the low risk nature of patient groups which have Clavien-Dindo I and II infection compared to the high-risk nature of those who develop grade III and above infection. These patient groups are likely to have more co-morbidities and confounding risk factors not taken into account in unadjusted analyses.

Development of post-operative infection was associated with mortality, particularly when patients developed CNS infections or peritonitis. This supports multiple studies which have previously reported associations between post-operative infection and mortality across surgical specialities.[33] The increased risk seen from our results are consistent with a previous study reporting that three-year mortality following radical cystectomy is 10.2% amongst patients developing surgical site infection compared to only 4.2% in non-infected patients.[34]

The strengths of our analyses are that we evaluated risk factors and patterns of development of various post-operative infection across a range of surgical specialities within a single large cohort. Our multi-centre study design and the large varied population make our results broadly generalisable to patients having non-cardiac surgery. The statistical analyses were pre-specified and multivariable models used to correct for confounding factors. However, the limitation of our study is the observational design. Many important factors were prospectively recorded, but there will be a degree of unmeasured confounding for example between cardiovascular risk factors and it is difficult to estimate how residual confounding may have altered our conclusions. We excluded patients with multiple infection events and patients categorised into more than one type of surgery when analysing the effect of each variable. Looking specifically between different types of infections resulted in smaller sample sizes in some categories, and so we have not assessed whether certain risk factors conferred a greater risk of various types of post-operative infection within surgical specialties. The true associations with individual risk factors remain unclear due to likely interactions between risk factors both from residual confounding and potential effect modification. For example, smoking history and co-morbidities including coronary artery disease and peripheral vascular disease, diabetes, or reduced renal function defined by lower eGFR and pre-operative anaemia defined by lower haemoglobin levels. Limitations of the dataset include incomplete data and lack of variables such as aggregated scoring systems to measure the burden of co-morbidities, frailty, socioeconomic status, elective versus emergency surgery. Surgical categories were also not able to be categorised by level of contamination.

Conclusions

We have described post-operative infection rates in a large international cohort of patients undergoing non-cardiac surgery. This has allowed us to provide accurate and generalisable estimates of the key risk factors for infection and subsequent patient outcomes. Infection is a common and important complication of non-cardiac surgery which is associated with high mortality. We have also shown an association with MINS but are unable to explore the underlying cause of this. New treatment approaches are needed to prevent infection which rely less on antimicrobial drugs and focus on better prevention strategies warranting further research. The risks of infection should be discussed with patients before surgery.

Author Contributions

Data collection: VISION group

Study design: All authors

Statistical analysis: YI Wan, A Patel

Drafting: YI Wan, RM Pearse

Critical review and approval of final manuscript: All authors

Declaration of Interests

RP holds research grants and has given lectures and/or performed consultancy work for Nestle Health Sciences, BBraun, Medtronic, Glaxo Smithkline, Intersurgical, and Edwards Lifesciences, and is a member of the Associate editorial board of the British Journal of Anaesthesia. GLA is a member of the editorial advisory board for Intensive Care Medicine Experimental, Editor for British Journal of Anaesthesia and has undertaken consultancy work for GlaxoSmithKline. ED was co-applicant on investigator-initiated research grants received from Roche Diagnostics and Abbott Diagnostics. All other authors declare no conflicts of interests. PJD is part of a group that has a policy of not accepting honorariums or other payments from industry for their own personal financial gain. Members of this group accept honoraria or other payments from industry to support research endeavours and for reimbursement of costs to participate in meetings such as scientific or advisory committee meetings. Based on study questions PJD originated and grants he wrote, he has received grants from Abbott Diagnostics, Astra Zeneca, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Covidien, Philips Healthcare, Stryker, and Roche Diagnostics. PJD has also participated in an advisory boarding meeting for GlaxoSmithKline and an expert panel meeting for Astra Zeneca.

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Table 1. Baseline characteristics for all patients, categorised by infection status. All data presented as n (%) unless otherwise specified, total n for variables with missing data listed as [n], SD – standard deviation, IQR – interquartile range. BMI – body mass index, Hb – haemoglobin, eGFR – estimated glomerular filtration rate. Current smoker defined as within 30 days before surgery. [1] 8 patients had missing infection outcome. [2] BMI were calculated using height and weight values, height outside of range 1.40-2.00 m and weight outside of range 40-150 kg were excluded for biological plausibility and to eliminate extreme outliers. [3] Hb values greater than 20.0 g dL^{-1} were also excluded for biological plausibility and to eliminate extreme outliers. [4] 1,165 patients had surgery which came under more than one category: 1,099 had two, 66 had three.

	All patients n=40004	**No infection [1] n=36091**	**Infection [1] n=3905**
Age in years			
Mean (SD)	64.0 (11.3)	63.7 (11.2)	66.8 (11.9)
Median (IQR)	63.2 (54.8-72.5)	62.9 (54.7-72.0)	66.4 (57.4-75.9)
<65	22141 (55.3)	20350 (56.4)	1786 (45.7)
65-85	16434 (41.1)	14570 (40.4)	1861 (47.7)
≥85	1429 (3.6)	1171 (3.2)	258 (6.6)
Sex			
Male	20127 (50.3)	18075 (50.1)	2047 (52.4)
Smoking status			
Never smoked	21195 (53.8)	19422 (54.6)	1766 (46.1)
Ex-smoker	12591 (32.0)	11124 (31.3)	1467 (38.3)
Current smoker	5615 (14.3)	5015 (14.1)	600 (15.7)
	[39401]	[35561]	[3833]
BMI [2]			
Underweight <18.5	1227 (3.3)	1042 (3.1)	185 (5.1)
Normal range 18.5 – 24.9	13327 (35.4)	12013 (35.3)	1311 (36.3)
Overweight ≥25	13093 (34.8)	11936 (35.1)	1154 (31.9)
Obese ≥30	9976 (26.5)	9012 (26.5)	964 (26.7)
	[37623]	[34003]	[3614]
Co-morbidities			
Current atrial fibrillation	1123 (2.8)	914 (2.5)	209 (5.4)
	[39876]	[35980]	[3889]
Previous atrial fibrillation	1262 (3.2)	1058 (2.9)	204 (5.3)
	[39827]	[35943]	[3878]
Congestive heart failure	1424 (3.6)	1182 (3.3)	241 (6.2)
	[39870]	[35973]	[3890]
Coronary artery disease	5159 (12.9)	4512 (12.5)	646 (16.6)
	[39876]	[35979]	[3890]
Cerebral vascular event	2582 (6.5)	2206 (6.1)	375 (9.6)
Peripheral vascular disease	3203 (8.0)	2748 (7.6)	455 (11.7)
Hypertension	20152 (50.5)	17933 (49.8)	2217 (56.9)
	[39917]	[36013]	[3897]
Chronic obstructive pulmonary disease	3165 (7.9)	2658 (7.4)	506 (13.0)
Diabetes	8332 (20.9)	7383 (20.5)	947 (24.3)
	[39905]	[36001]	[3897]
Active cancer	6168 (15.4)	5333 (14.8)	834 (21.4)
	[40002]	[36091]	[3903]
Pre-operative Hb level in g dL^{-1} [3]			
Mean (SD)	13.0 (2.0)	13.1 (1.9)	12.5 (2.1)
Median (IQR)	13.2 (11.9-14.3)	13.2 (12.0-14.4)	12.7 (11.0-14.0)
	[38614]	[34769]	[3841]
Pre-operative eGFR			
<30	1515 (4.1)	1265 (3.8)	250 (6.7)
30-44	1774 (4.8)	1512 (4.5)	262 (7.0)
45-60	3707 (9.9)	3262 (9.7)	444 (11.9)
>60	30294 (81.2)	27499 (82.0)	2792 (74.5)
	[37290]	[33538]	[3748]
Urgency of surgery			
<72 hours since acute event	4189 (10.5)	3585 (9.9)	604 (15.5)
All other surgeries	35815 (89.5)	32506 (90.1)	3301 (84.5)

Type of surgery [4]			
Vascular	2642 (6.6)	2354 (6.5)	287 (7.4)
	[39997]	[36085]	[3904]
General	7950 (19.9)	6549 (18.2)	1400 (35.9)
Thoracic	1165 (2.9)	1074 (3.0)	91 (2.3)
Major urology or gynaecology	4827 (12.1)	4407 (12.2)	420 (10.8)
Major orthopaedic	6982 (17.5)	6216 (17.2)	764 (19.6)
Major neurosurgery	2341 (5.9)	2114 (5.9)	227 (5.8)
Low risk surgery	15308 (38.3)	14394 (39.9)	910 (23.3)
Surgical technique			
Endoscopic only	8683 (21.7)	8167 (22.6)	516 (13.2)
Open	31288 (78.3)	27901 (77.4)	3381 (86.8)
	[39971]	[36066]	[3899]
Type of anaesthetic			
General	27069 (69.3)	24164 (68.6)	2903 (75.4)
Regional	10005 (25.6)	9218 (26.2)	786 (20.4)
Combined	1997 (5.1)	1836 (5.2)	161 (4.2)
	[39071]	[35218]	[3850]

Table 2. Baseline characteristics for patients with infection, categorised by infection type. All data presented as n (%) unless otherwise specified, total n for variables with missing data listed as [n], SD – standard deviation, IQR – interquartile range. BMI – body mass index, UTI – urinary tract infection, URTI – upper respiratory tract infection, CNS – central nervous system. Current smoker defined as within 30 days before surgery. [1] BMI were calculated using height and weight values, height outside of range 1.40-2.00 m and weight outside of range 40-150 kg were excluded for biological plausibility and to eliminate extreme outliers. [2] Hb values greater than 20.0 g dL^{-1} were also excluded for biological plausibility and to eliminate extreme outliers. Note a number of patients had incidences of more than one infection: 590 had two, 164 had three, 49 had four, 30 had five, three had six, three had seven, three has eight and one had nine. Only the infection event with the highest severity grading was included for each patient. [3] 1,165 patients had surgery which came under more than one category: 1,099 had two, 66 had three. An extended table including co-morbidities, pre-operative haemoglobin level, estimated glomerular filtration rate, surgical technique is included in the supplement.

	Surgical incision n=1555	Surgical abscess n=340	UTI n=1086	URTI n=101	Pneumonia n=771	Peritonitis n=134	Osteomyelitis n=29	CNS n=33	Blood culture n=115	Other n=761
Age in years										
Mean (SD)	64.9 (11.4)	63.7 (10.9)	70.0 (12.4)	68.2 (10.9)	63.9 (11.3)	66.2 (11.7)	63.4 (13.4)	56.9 (9.5)	65.9 (11.9)	66.5 (11.8)
Median (IQR)	64.5 (55.8-73.6)	63.2 (54.9-72.3)	71.0 (60.9-79.5)	67.8 (61.3-76.4)	63.1 (54.8-72.4)	66.5 (57.4-74.9)	61.2 (51.0-75.6)	56.5 (49.1-60.3)	65.6 (55.7-74.9)	65.9 (57.4-74.7)
<65	799 (51.4)	196 (57.7)	378 (34.8)	40 (39.6)	310 (40.2)	59 (44.0)	19 (65.5)	27 (81.8)	55 (47.8)	351 (46.1)
65-85	702 (45.1)	135 (39.7)	583 (53.7)	54 (53.5)	403 (52.3)	69 (51.5)	8 (27.6)	6 (18.2)	53 (46.1)	365 (48.0)
≥85	54 (3.5)	9 (2.7)	125 (11.5)	7 (6.9)	58 (7.5)	6 (4.5)	2 (6.9)	0 (0)	7 (6.1)	45 (5.9)
Sex										
Male	836 (53.8)	188 (55.3)	422 (38.9)	70 (69.3)	474 (61.5)	87 (64.9)	22 (75.9)	14 (42.4)	69 (60.0)	435 (57.2)
Smoking status										
Never smoked	703 (46.0)	155 (46.0)	547 (51.1)	26 (27.1)	307 (41.0)	50 (37.9)	14 (50.0)	26 (86.7)	55 (49.6)	315 (42.3)
Ex-smoker	573 (37.5)	97 (38.3)	408 (38.1)	47 (49.0)	302 (40.4)	56 (42.4)	10 (35.7)	3 (10.0)	39 (35.1)	303 (40.7)
Current smoker	254 (16.6)	53 (15.7)	115 (10.8)	23 (24.0)	139 (18.6)	26 (19.7)	4 (14.3)	1 (3.3)	17 (15.3)	126 (16.9)
	[1530]	[337]	[1070]	[96]	[748]	[132]	[28]	[30]	[111]	[744]
BMI [1]										
Underweight <18.5	65 (4.5)	12 (3.7)	45 (4.5)	2 (2.2)	66 (9.3)	7 (5.6)	0 (0)	0 (0)	3 (2.8)	39 (5.6)
Normal range 18.5–24.9	478 (33.1)	138 (42.6)	364 (36.2)	34 (37.0)	285 (40.2)	48 (38.1)	8 (32.0)	11 (50.0)	37 (34.3)	248 (35.4)
Overweight ≥25	445 (30.8)	95 (29.3)	346 (34.4)	30 (32.6)	203 (28.6)	41 (32.5)	9 (36.0)	4 (18.2)	44 (40.7)	228 (32.5)
Obese ≥30	456 (31.6)	79 (24.4)	250 (24.9)	26 (28.3)	155 (21.9)	30 (23.8)	8 (32.0)	7 (31.8)	24 (22.2)	186 (26.5)
	[1444]	[324]	[1005]	[92]	[709]	[126]	[25]	[22]	[108]	[701]
Urgency of surgery										
<72 hours since acute event	203 (13.1)	35 (10.3)	191 (17.6)	9 (8.9)	167 (21.7)	39 (29.1)	4 (13.8)	9 (27.3)	15 (13.0)	115 (15.1)
All other surgeries	1352 (87.0)	305 (89.7)	895 (82.4)	92 (91.1)	604 (78.3)	95 (70.9)	25 (86.2)	24 (72.7)	100 (87.0)	646 (84.9)
	[1555]	[340]	[1086]	[101]	[771]	[134]	[29]	[33]	[115]	[761]
Type of surgery [3]										
Vascular	116 (7.5)	9 (2.7)	57 (5.3)	11 (10.9)	65 (8.4)	3 (2.2)	1 (3.5)	1 (3.0)	10 (8.7)	81 (10.6)
	[1555]	[339]	[1086]	[101]	[771]	[134]	[29]	[33]	[115]	[761]
General	576 (37.0)	221 (65.0)	308 (28.4)	43 (42.6)	292 (37.9)	111 (82.8)	2 (6.9)	1 (3.0)	41 (35.7)	282 (37.1)

	[1555]	[340]	[1086]	[101]	[771]	[134]	[29]	[33]	[115]	[761]
Thoracic	20 (1.3)	3 (0.9)	13 (1.2)	2 (2.0)	54 (7.0)	1 (0.8)	0 (0)	0 (0)	5 (4.4)	22 (2.9)
	[1555]	[340]	[1086]	[101]	[771]	[134]	[29]	[33]	[115]	[761]
Major urology or gynaecology	141 (9.1)	39 (11.5)	200 (18.4)	5 (5.0)	56 (7.3)	5 (3.7)	0 (0)	0 (0)	9 (7.8)	68 (8.9)
	[1555]	[340]	[1086]	[101]	[771]	[134]	[29]	[33]	[115]	[761]
Major orthopaedic	307 (19.7)	21 (6.2)	278 (25.6)	11 (10.9)	126 (16.3)	0 (0)	11 (37.9)	2 (6.1)	19 (16.5)	134 (17.6)
	[1555]	[340]	[1086]	[101]	[771]	[134]	[29]	[33]	[115]	[761]
Major neurosurgery	56 (3.6)	11 (3.2)	81 (7.5)	12 (11.9)	72 (9.3)	1 (0.8)	2 (6.9)	13 (39.4)	8 (7.0)	44 (5.8)
	[1555]	[340]	[1086]	[101]	[771]	[134]	[29]	[33]	[115]	[761]
Low risk surgery	415 (26.7)	56 (16.5)	234 (21.6)	19 (18.8)	145 (18.8)	16 (11.9)	13 (44.8)	18 (54.6)	24 (20.9)	154 (20.2)
	[1555]	[340]	[1086]	[101]	[771]	[134]	[29]	[33]	[115]	[761]
Type of anaesthetic										
General	1118 (73.2)	291 (86.9)	773 (71.8)	83 (82.2)	630 (82.8)	125 (94.0)	12 (42.9)	33 (100)	97 (84.4)	591 (78.9)
Regional	343 (22.5)	33 (9.9)	265 (24.6)	15 (14.9)	103 (13.5)	5 (3.8)	13 (46.4)	0 (0)	12 (10.4)	127 (17.0)
Combined	67 (4.4)	11 (3.3)	38 (3.5)	3 (3.0)	28 (3.7)	3 (2.3)	3 (10.7)	0 (0)	6 (5.2)	31 (4.1)
	[1528]	[335]	[1076]	[101]	[761]	[133]	[28]	[33]	[115]	[749]